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Case report

Taurolidine as adjuvant treatment of relapsing peritonitis in peritoneal dialysis patients☆

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ABSTRACT

Relapsing peritonitis in peritoneal dialysis patients is one of the complications that jeopardises the continuity of the technique. It is often associated with the formation of biofilm in the lumen of the catheter. To date, its removal remains the only recommended attitude. Due to its antimicrobial and antifungal properties, taurolidine has been previously used for the sealing of central line catheters and hemodialysis. Despite the good results obtained, there is no evidence available regarding its utility in peritoneal dialysis.

This case report describes the use of taurolidine (TauroLock™ HEP 500) in 5 patients with relapsing peritonitis after antibiotic treatment completion. Mean follow-up for the detection of recurrences was 13.4 months. In 4 patients with infections caused by *Staphylococcus epidermidis*, eradication was achieved. In the remaining case, caused by *Staphylococcus aureus*, the taurolidine seal was ineffective and the removal of the catheter was required.

Taurolidina como tratamiento adyuvante en casos de peritonitis recidivante en pacientes en diálisis peritoneal

Palabras clave:
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RESUMEN

La peritonitis recidivante en pacientes en diálisis peritoneal es una de las complicaciones que ponen en riesgo la continuidad de la técnica. Se asocia a menudo con la formación de biofilm en la luz del catéter. Hasta la fecha, su retirada sigue siendo la única actitud recomendada. Debido a sus propiedades antimicrobianas y antifúngicas, se ha utilizado taurolidina para el sellado de catéteres de vías centrales y de hemodiálisis. A pesar de los buenos resultados obtenidos, no existen datos sobre su utilidad en diálisis peritoneal.

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Se presentan 5 casos de peritonitis recidivante en los que se utilizó sellado con taurolidina (TauroLock™ HEP 500) tras cumplir tratamiento antibiótico. Se realizó un seguimiento medio de 13,4 meses para la detección de recidivas. En 4 pacientes con infecciones provocadas por *Staphylococcus epidermidis* se consiguió la erradicación. En el caso restante, causado por *Staphylococcus aureus,* el sellado con taurolidina fue inefectivo y precisó la retirada del catéter.

Introduction

Relapsing peritonitis is defined as a new episode of peritoneal infection caused by the same organism less than four weeks after completion of the previous treatment. In patients on peritoneal dialysis (PD), it has a lower cure rate and is associated with deficient ultrafiltration and increased risk of dialysis failure.[1] It is often caused by the formation of biofilm within the lumen of the catheter. The layer of exopolysaccharides produced by the bacteria prevents an appropriate penetration of antimicrobial agents and it is very difficult to eradicate.[2] Even though there are studies on adjuvant treatments, the International Society for Peritoneal Dialysis (ISPD) recommends catheter removal in the case of relapsing peritonitis.[1,3,4] This means that the patient has to discontinue to leave the peritoneal dialysis programme temporarily, or may need to be changed definitively to haemodialysis.

A derivative of taurine called taurolidine has been proven to be effective in eradicating biofilms caused by both Gram-positive and Gram-negative bacteria and *Candida albicans*.[5] On that basis, its use has been extended as a lock for central and parenteral nutrition lines and haemodialysis catheters for prevention of bacteraemia.[6–8] In spite of the positive results, there is little experience of its use in PD. With its broad antimicrobial spectrum, it could be a therapeutic alternative in relapsing or recurrent peritonitis related to biofilm formation.

We present our experience of locking with taurolidine in five patients with relapsing peritonitis treated in our PD Unit from January 2016 to July 2018. The compound used was TauroLock™ HEP 500 (taurolidine-citrate 4% combined with heparin).

Case reports

We report the cases of five male patients in the PD programme with surgically implanted catheters. All had been trained correctly before starting home dialysis. The mean time from starting PD to the first episode of relapsing peritonitis was 16.4 months. The clinical characteristics of the patients are shown in Table 1. A two-week course of intraperitoneal vancomycin was the treatment of choice, as per the antibiogram, in all five cases. Their levels were checked periodically. Between the episodes of peritonitis, the adequacy of each patient's dialysis technique was re-assessed by the PD Unit nurse. In none of the cases was observed exit site infection of the peritoneal catheter.

The locking was carried out with TauroLock™ HEP after completing the antibiotic treatment (using the exact volume of the peritoneal catheter), with caution on having a full abdomen to avoid possible pain during the infusion. The infusion was administered very slowly and the catheter remained locked for 12 h. As the treatment was always to be administered in the clinic, two distinct protocols were established, depending on whether the patient was on automated peritoneal dialysis (APD) or continuous ambulatory peritoneal dialysis (CAPD). Both protocols are shown in Table 2.

The lock with taurolidine was effective in 80% of the cases. The cases of peritonitis caused by *Staphylococcus epidermidis* did not relapse again regardless of the dialysis technique used. To date, the patients have had no further episodes of peritonitis caused by the same organism. The average subsequent follow-up time was 13.4 months. No side effects were recorded over the course of the treatment.

Patient number five had positive cultures for *Staphylococcus aureus* despite the taurolidine lock. He was given oral rifampicin and an additional urokinase lock was performed, but without success. A change of antibiotic combining daptomycin, both for catheter locking and intravenous administration, did not produce the expected results. Finally, the patient had to have the catheter removed and be changed to haemodialysis. Unfortunately, he died a few months later as a result of sepsis of soft-tissue.

Discussion

Despite multiple attempts to save peritoneal catheters in cases of relapsing peritonitis, withdrawal is often the only recommendation.[1] In a retrospective study with the combination of intraperitoneal urokinase and oral rifampicin, Demoulin and Goffin managed to maintain 64% of peritoneal catheters in asymptomatic peritonitis due to coagulase-negative staphylococci.[3] However, the benefits of intraperitoneal urokinase in refractory peritonitis has not been confirmed in randomised trials.[9,10] For *S. aureus* peritonitis, a reduction in the risk of relapse has been reported with the use of adjuvant rifampicin for 5–7 days.[11] This treatment option failed in our patient number five. There are also series described in the literature of relapsing peritonitis treated successfully with antibiotic locks, but more studies are needed in order to extend this procedure.[2,12]

Presently, there is little evidence on the utility of taurolidine in PD. Gallieni et al. published a case of fungal peritonitis treated with intraperitoneal taurolidine washes that failed

Table 1 – Clinical characteristics of the patients.

No.	Age (years)	Type of technique	Type of peritoneal catheter	Time from start of PD to 1st episode of peritonitis (months)	Organism	Date of previous episodes of peritonitis	Antibiotic therapy	Follow-up time after taurolidine lock (months)	New episodes of peritonitis after taurolidine lock	Removal of peritoneal catheter
1	67	CAPD	Swan-neck straight-tip	34	*S. epidermidis*	Jun-17 Jul-17 Sept-17	IP Vancomycin (14 d) IP Vancomycin (14 d) IP Vancomycin (14 d) + TauroLock-Hep	10	No	No
2	69	CAPD	Swan-neck straight-tip	12	*S. epidermidis*	Apr-17 May-17 Sept-17	IP Vancomycin (14 d) IP Vancomycin (14 d) + urokinase lock IP Vancomycin (14 d) + TauroLock-Hep	10	No	No
3	72	APD	Swan-neck straight-tip	8	*S. epidermidis*	Oct-15 Jan-16 Mar-16 Apr-16	IP Vancomycin (14 d) IP Vancomycin (14 d) IP Vancomycin (14 d) IP Vancomycin (14 d) + TauroLock-Hep	28	No	No
4	60	CAPD	Swan-neck straight-tip	11	*S. epidermidis*	Apr-16 May-16 Jun-16	IP Vancomycin (14 d) IP Vancomycin (14 d) IP Vancomycin (14 d) + TauroLock-Hep	13	No	No
5	85	CAPD	Swan-neck pigtail-curled	17	*S. aureus*	Feb-16 Mar-16 Apr-16 Jul-16 Aug-16	IP Vancomycin (14 d) IP Vancomycin (14 d) IP Vancomycin (14 d) + TauroLock-Hep IP Vancomycin + oral rifampicin (14 d) + urokinase lock IV Daptomycin + daptomycin lock (15 d)	6	Yes	Yes

APD: automated peritoneal dialysis; CAPD: continuous ambulatory peritoneal dialysis; d: days; IP: intraperitoneal; IV: intravenous; PD: peritoneal dialysis.

Table 2 – Taurolidine administration protocol according to peritoneal dialysis technique.

Type of technique	Protocol
APD	Catheter locked with exact volume of TauroLock™ HEP 500 during daytime exchange (minimum time to remain *in situ* 12 h) Locked daily for the first five days and then twice a week for four weeks
CAPD	Catheter locked with exact volume of TauroLock™ HEP 500 during exchange with icodextrin or glucose solution (minimum time to remain *in situ* 12 h) Locked twice a week for four weeks

APD: automated peritoneal dialysis; CAPD: continuous ambulatory peritoneal dialysis.

due to the intense pain caused during the procedure.[13] Two cases of relapsing peritonitis due to *S. epidermis* and *Micrococcus luteus* treated by taurolidine lock have been reported with good results.[14] In our series, locking with taurolidine prevented relapse in all the cases caused by *S. epidermidis*, but it was not effective in the case of *S. aureus*. This situation could be explained by extrapolating the results of the work of Liu et al.[15]: in this meta-analysis of three trials on the prevention of bacteraemia with taurolidine solution, no significant differences were found in the incidence of Gram-positive infections, but significant differences were found in Gram-negative infections. However, the majority of cases in the above study were caused by *S. aureus*.[16–18] It should be noted that in our series, we only treated one case of peritonitis due to *S. aureus*, so a larger sample size would be required to draw conclusions. One study with paediatric patients with cancer found a significant reduction in central access infections caused by coagulase-negative staphylococci and methicillin-resistant *S. epidermidis* through the use of taurolidine-citrate.[19]

Because of the few publications on its use in PD, there is no evidence regarding the appropriate administration protocol. Based on the premises of maintaining the lock for at least 12 h and administering the solution in the clinic, the two aforementioned protocols were established. Ideally, it was considered that the locking should be daily and that it would not be a problem in APD. In the case of patients on CAPD, on the day of applying the lock, only two exchanges could be made (no interference with night-time rest). This would make daily treatment difficult because of the risk of under-dialysis, so in the first week only two treatments were given *versus* the five in the patients on APD. As an additional measure, the day after locking they were advised to carry out an additional exchange over their prescribed regimen. In view of the results, given that the majority of patients were on CAPD, this protocol (with a lower number of doses) could also be applied to patients on APD.

The results from this series are promising. Nevertheless, the small sample size is a limitation from the point of view of generalised use of this treatment in routine clinical practice. Prospective controlled and randomised studies with larger samples would be necessary to confirm these findings.

Conclusions

The taurolidine solution was effective in four out of five of our patients with relapsing peritonitis. It prevented new episodes of peritonitis in all cases caused by *S. epidermidis*. No adverse effects were recorded with this treatment. Larger, randomised studies are needed to be able to make recommendations with better evidence.

Conflicts of interest

The authors have no conflicts of interest to declare.

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